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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/501,183

10/07/2006

Costas N. Karatzas

9529-008-999

6046

20583

7590

09/18/2008

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER

KAM, CHIH MIN

ART UNIT

PAPER NUMBER

1656

MAIL DATE

DELIVERY MODE

09/18/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,183	KARATZAS ET AL.	
	Examiner	Art Unit	
	CHIH-MIN KAM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 6/6/08.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-41 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 and 21-41 is/are rejected.
- 7) ☒ Claim(s) 20 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 7/9/04 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9/25/07</u> . | 6) <input checked="" type="checkbox"/> Other: <u>sequence match</u> . |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of species of: (1) SEQ ID NO:12 (AAAAAAAA), and corresponding (A)_n; (2) repetitive unit of MaSpI, having an amino acid sequence of SEQ ID NO:1; (3) non-repetitive unit of MaSpI; and (4) additional peptide sequence of a secretory signal peptide sequence in the response to restriction requirement filed June 6, 2008 is acknowledged. The traversal is on the ground(s) that while the Patent Office alleged the species are "patentably distinct due to their mutually exclusive characteristics", the Office has not explained why the differences, say, between iterated peptide motifs AAAAA (SEQ ID NO:4), GAGA (SEQ ID NO:6), GAGAGA (SEQ ID NO:7) and AAAAAAAAA (SEQ ID NO:12), amount to patentable distinct difference since any single repetitive unit typically includes more than one type of iterated peptide motif, e.g., repetitive unit MaSpI comprises iterated peptide motifs such as (GA)_n and A_n. Applicants' response has been considered. However, the arguments are not persuasive because each silk polypeptide, which contains different iterated peptide motif (e.g., AAAAA vs. GAGA), would have different amino acid sequence and different physical properties, thus each silk polypeptide is patentably distinct. Upon reconsideration, species of ADF-1, ADF-2, ADF-3, ADF-4, ABF-1, MaSpI, MaSpII, MiSpI, MiSpII and Flag as repetitive unit (claim 19), species of MaSpI, MaSpII, ABF-1, ADF-1, ADF-2, ADF-3, ADF-4, and Flag as non-repetitive hydrophilic carboxy terminal region (claim 31), and species of additional peptide sequence of c-myc epitope (claim 38), and his tag (claim 39) are included for examination.

The requirement is still deemed proper and is therefore made FINAL. Therefore, claims 1-41 and elected species are examined.

Informalities

The disclosure is objected to because of the following informalities:

2. Figs. 5-10 and the specification (e.g., page 35, line 24; page 40, lines 34-35) recite amino acid sequences, however, these sequences are not identified by "SEQ ID NO:". Applicant must comply with the requirements of sequence rules (37 CFR 1.821-1.825) to identify all the sequences in the specification and to include all the sequences in the sequence listing. Appropriate correction is required.
3. The specification recites a PCT application without providing the application number. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-19 and 21-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-19 and 21-41 are directed to an isolated silk polypeptide comprising a plurality of repetitive units and a non-repetitive hydrophilic amino acid domain.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

While the specification discloses that a silk polypeptide comprising a plurality of repetitive units and a non-repetitive hydrophilic amino acid domain, where the repetitive units can be selected from the group consisting of ADF-1, ADF-2, ADF-3, ADF-4, ABF-1, MaSpI, MaSpII, MiSpI, MiSpII and Flag, or the repetitive units can be the amino acid sequence of SEQ ID NO:1, 2 or 3; and the non-repetitive hydrophilic amino acid domain can be selected from the group consisting of non-repetitive hydrophilic carboxyl terminal region of MaSpI, MaSpII, MiSpI, MiSpII, ADF-1, ADF-2, ADF-3, ADF-4, ABF-1,

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NCF-1, NCF-2, and Flag (pages 3-5), the specification does not disclose a genus of variants of silk polypeptides comprising a plurality of repetitive units and a non-repetitive hydrophilic amino acid domain, when there is substantial variation within the genus. A few species of silk polypeptides of SEQ ID NO:1, 2 and 3 do not provide sufficient written description for the genus of variants of silk polypeptides comprising a plurality of repetitive units and a non-repetitive hydrophilic amino acid domain, where the sequences of repetitive units and a non-repetitive hydrophilic amino acid domain are not defined. Without guidance on structure to function/activity of various silk polypeptides, one skilled in the art would not know what polypeptides can be identified as silk polypeptides. The lack of description on the structure to function/activity relationship of various silk polypeptides, and the lack of representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-3, 6-8, 10, 11, 15-19, 22-26, 30, 31, 39 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Prince *et al.* (Biochemistry 34, 10879-10885 (1995), listed as C10 in IDS filed 9/25/07).

Prince *et al.* teach synthetic genes encoding recombinant spider silk proteins have been constructed, cloned and expressed, where the silk protein sequences are derived from *Nephila clavipes*, and DNA “monomer” sequences multimerized (from 1 to 18 repeats) to encode high molecular weight synthetic spider silk proteins such as [SPI]₄ (14.7 kDa), [SPI]₇ (23.5 kDa), [SPI]₁₀ (32.4 kDa) and [SPI]₁₃ (41.3 kDa) using a “head-to-tail” construction strategy (Table 1; page 10882; claims 1-3, 6-8, 10, 11, 16, 17, 23, 31 and 40). The reference also discloses a [His]₆ sequence is placed at the N-terminus of the recombinant protein for purification (page 10882, left column; claim 39), and the amino acid sequence of [SPI] (Fig. 1;

SGRGGLGGQGAGAAAAAAGGAGQGGYGGLGSQGT) contains repetitive units of A_n (claims 18, 19, 22, 24-26, 30). The relative proportions of secondary structure were estimated at 55% b-sheet structure and 39% random coil for [SPI]₄ and 65% b-sheet structure and 27% random coil for [SPI]₇ (page 10883; fig. 4; claim 15).

6. Claims 1, 6-8, 16-19, 22-26, 30, 32, 37 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Lewis *et al.* (U.S. Patent 5,756,677, listed as A01 in IDS filed 9/25/07).

Lewis *et al.* teach cloned cDNA obtained from the minor ampullate gland of *Nephila clavipes* encodes minor ampullate spidroin proteins (MiSP), and the translated MiSPs have a structure which exhibits an amino proximal nonrepetitive region, a repetitive portion and a carboxy-proximal nonrepetitive portion (Example 1; claims 1, 16, 17, 19, 25, 26, 30), where the spider silk protein has a molecular weight of at least 16 kDa, preferably 120 kDa to 300 kDa for the full length (column 2, lines 1-4; column 3, lines 7-41; Fig. 4; claim 40). The nucleotide sequence and the protein sequence of

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MiSP1 has been shown in Figs. 1A-1E, and the nucleotide sequence and the protein sequence of MiSP2 has been shown in Figs. 2A-2D (Example 1), in which the 5'-nonrepetitive region contains a sequence of about 16 residues (amino acids 2-17) that conforms secretion signal sequence (claim 37), and Table 1 shows the MiSPI amino acid sequence shows 13 unit repeats, including (A)_n (column 5; claim 6-8, 18, 22-24, 32).

Claim Objections

7. Claim 20 is objected to as being dependent upon a rejected base claim.

Conclusion

8. Claims 1-19 and 21-41 are rejected; and claim 20 is objected to.

Art of record

Beckwitt *et al.* (J. Biol. Chem. 269, 6661-6663; reference C01 in IDS filed 9/25/07) disclose the amino acid sequence of dragline silk protein spidroin 1 has 95.2% sequence identity to the amino acid sequence of SEQ ID NO:1 (see attached sequence match).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Chih-Min Kam/

Primary Examiner, Art Unit 1656

CMK

September 12, 2008